

Rule
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vessel length in the mammal.

~~8~~
The method of claim 6, wherein the increase in blood vessel length is at least about 5% as determined by a standard blood vessel length assay.

~~9~~
The method of claim 6, wherein the amount of vascularization modulating agent administered to the mammal is further sufficient to increase blood vessel diameter in the mammal.

~~10~~
The method of claim 9, wherein the increase in blood vessel diameter is at least about 5% as determined by a standard blood vessel diameter assay.

~~11~~
The method of claim 1, wherein the amount of vascularization modulating agent administered to the mammal is sufficient to increase EPC differentiation following tissue ischemia.

~~12~~
The method of claim 10, wherein the increase in EPC differentiation is at least about 20% as determined by a standard hindlimb ischemia assay.

~~13~~
The method of claim 1, wherein the amount of administered vascularization modulating agent is sufficient to increase neovascularization by at least about 5% as determined by a standard cornea micropocket assay.

~~14~~
The method of claim 1, wherein the amount of administered vascularization modulating agent is sufficient to increase EPC bone marrow

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~~14. The method of claim 13, wherein the increase in EPC bone marrow derived EPC incorporation into foci is at least about 20% as determined by a standard rodent bone marrow (BM) transplantation model.~~

16 The method of claim 15, wherein the ischemic tissue is associated with an ischemic vascular disease.

~~18~~ The method of claim 15, wherein the tissue is associated with the circulatory system or the central nervous system.

~~20~~ The method of claim 1, wherein the is co-administered with at least one angiogenic protein.

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22. The method of claim 20, wherein the angiogenic protein is
acidic fibroblast growth factor (aFGF), basic fibroblast growth factor (bFGF),
vascular endothelial growth factor (VEGF-1), epidermal growth factor (EGF),
5 transforming growth factor α and β (TGF- α and TGF- β), platelet-derived
endothelial growth factor (PD-ECGF), platelet-derived growth factor (PDGF),
tumor necrosis factor α (TNF- α), hepatocyte growth factor (HGF), insulin like
- growth factor (IGF), erythropoietin, colony stimulating factor (CSF),
macrophage-CSF (M-CSF), angiopoietin-1 (Ang1) or nitric oxidesynthase
10 (NOS); or a fragment thereof.

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23. The method of claim 22, wherein the protein is one of VEGF-B,
VEGF-C, VEGF-2, VEGF-3; or an effective fragment thereof.

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24. A method for preventing or reducing the severity of blood
vessel damage in a mammal, wherein the method comprises administering to
the mammal an effective amount of granulocyte macrophage-colony
stimulating factor (GM-CSF); and exposing the mammal to conditions
conductive to damaging the blood vessels, the amount of GM-CSF being
20 sufficient to prevent or reduce the severity of the blood vessel damage in the
mammal.

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25. The method of claim 24, wherein the conditions conducive to
the blood vessel damage are an invasive manipulation or ischemia.

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26. The method of claim 25, wherein the invasive manipulation is
surgery.

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27. The method of claim 25, wherein the ischemic is associated

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with at least one of infection, trauma, graft rejection, cerebrovascular ischemia, renal ischemia, pulmonary ischemia, limb ischemia, ischemic cardiomyopathy, or myocardial ischemia.

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~~28~~ The method of claim 24, wherein the GM-CSF is administered to the mammal at least about 12 hours before exposing the mammal to the conditions conducive to damaging the blood vessels.

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~~30~~
~~29~~ The method of claim 28, wherein the GM-CSF is administered to the mammal between from about 1 to 10 days before exposing the mammal to the conditions conducive to damaging the blood vessels.

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~~31~~
~~30~~ The method of claim 28, wherein the method further comprises administering the GM-CSF to the mammal following the exposure to the conditions conducive to damaging the blood vessels.

~~32~~
~~31~~ A method for treating ischemic tissue in a mammal in need of such treatment, wherein the method comprises:

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- a) isolating endothelial progenitor cells (EPCs) from the mammal,
- b) contacting the isolated EPCs with an amount of an angiogenic protein sufficient to induce proliferation of the EPCs; and
- c) administering the proliferated EPCs to the mammal in an amount sufficient to treat the ischemic tissue.

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~~33~~
~~32~~ The method of claim 31, wherein the EPCs have at least one of the following markers: CD34⁺, flk-1⁺ or tie-2⁺

~~34~~
~~33~~ The method of claim 31, wherein the ischemic tissue comprises injured blood vessels.

~~35~~
~~34~~ The method of claim 33, wherein the blood vessels are injured
5 by an invasive manipulation.

~~36~~
~~35~~ The method of claim 34, wherein the invasive manipulation is balloon angioplasty, or deployment of a stent or catheter.

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~~36~~ The method of claim 35, wherein the stent is an endovascular
10 stent.

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~~37~~ The method of claim 31 further comprising co-administering at
least one angiogenic protein.

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~~38~~ The method of claim 37, wherein the angiogenic protein is an
15 endothelial cell mitogen or a nucleic acid encoding the endothelial cell mitogen.

~~40~~
~~39~~ The method of claim 38, wherein the angiogenic protein is
20 acidic fibroblast growth factor (aFGF), basic fibroblast growth factor (bFGF),
vascular endothelial growth factor (VEGF-1), epidermal growth factor (EGF),
transforming growth factor α and β (TGF- α and TGF- β), platelet-derived
endothelial growth factor (PD-ECGF), platelet-derived growth factor (PDGF),
25 tumor necrosis factor α (TNF- α), hepatocyte growth factor (HGF), insulin like
growth factor (IGF), erythropoietin, colony stimulating factor (CSF),
macrophage-CSF (M-CSF), angiopoietin-1 (Ang1) or nitric oxidesynthase
(NOS); or a fragment thereof.

~~41~~
~~40.~~ The method of claim 39, wherein the protein is one of VEGF-B, VEGF-C, VEGF-2, VEGF-3; or a fragment thereof.

5 ~~42~~
~~41.~~ A method for detecting presence of tissue damage in a mammal, wherein the method comprises contacting the mammal with a detectably-labeled population of endothelial progenitor cells (EPCs); and detecting the labeled cells at or near the site of the tissue damage in the mammal.

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~~42.~~ The method of claim 41, wherein the tissue damage is ischemia or an ischemic vascular disease.

~~44~~
~~43.~~ A pharmaceutical product for inducing neovascularization in a mammal, wherein the product comprises isolated endothelial progenitor cells (EPCs) and is formulated to be physiologically acceptable to a mammal.

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~~45~~
~~44.~~ The pharmaceutical product of claim 43, wherein the product is sterile and further comprises at least one angiogenic protein or nucleic acid encoding the protein.

20 ~~46~~
~~45.~~ A kit for the systemic introduction of a isolated endothelial progenitor cells (EPCs), wherein the kit comprises the isolated EPCs and optionally at least one angiogenic protein or nucleic acid encoding same, the kit further optionally comprising a pharmacologically acceptable carrier

25 solution, nucleic acid or mitogen, means for delivering the EPCs and directions for using the kit.

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